Therapeutic efficacy of cardiosphere-derived cells in a transgenic mouse model of non-ischaemic dilated cardiomyopathy.

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Public Summary:
Cardiosphere-derived cells (CDCs) produce regenerative effects in the post-infarct setting. However, it is unclear whether CDCs are beneficial in non-ischaemic dilated cardiomyopathy (DCM). We tested the effects of CDC transplantation in mice with cardiac-specific Galphaq overexpression, which predictably develop progressive cardiac dilation and failure, with accelerated mortality.

Scientific Abstract:
AIM: Cardiosphere-derived cells (CDCs) produce regenerative effects in the post-infarct setting. However, it is unclear whether CDCs are beneficial in non-ischaemic dilated cardiomyopathy (DCM). We tested the effects of CDC transplantation in mice with cardiac-specific Galphaq overexpression, which predictably develop progressive cardiac dilation and failure, with accelerated mortality. METHODS AND RESULTS: Wild-type mouse CDCs (10(5) cells) or vehicle only were injected intramyocardially in 6-, 8-, and 11-week-old Galphaq mice. Cardiac function deteriorated in vehicle-treated mice over 3 months of follow-up, accompanied by oxidative stress, inflammation and adverse ventricular remodelling. In contrast, CDCs preserved cardiac function and volumes, improved survival, and promoted cardiomyogenesis while blunting Galphaq-induced oxidative stress and inflammation in the heart. The mechanism of benefit is indirect, as long-term engraftment of transplanted cells is vanishingly low. CONCLUSIONS: Cardiosphere-derived cells reverse fundamental abnormalities in cell signalling, prevent adverse remodelling, and improve survival in a mouse model of DCM. The ability to impact favourably on disease progression in non-ischaemic heart failure heralds new potential therapeutic applications of CDCs.